GlaxoWellcome

June 5, 2000

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Management Dockets
Dockets Management Branch
Food and Drug Administration
HFA-305, Room 1-23
5630 Fishers Lane, Rm 1061
Rockville, MD 20852

Re: ICH QIA (R) Stability Testing of New Drug Substances and Products

Dear Dr. Dockets:

Please find enclosed Glaxo Wellcome's comments on the revised draft guidance Stability Testing of New Drug Substances and Products (ICH QIA).

Please feel free to contact me at (919) 483-9804 if you need additional information or clarification.

Sincerely,

Kimberley Jessup-Crippen

Kimberley Jessup-Crippen
US CMC Submissions
Chemistry Pharmacy and Manufacturing Regulatory Affairs and Quality Division

00N-1220

C3

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Comments from Glaxo Wellcome on
International Conference on Harmonization: Draft Revised Guidance on Q1A(R): Stability Testing of New Drug Substances and Products

Intermediate Storage Condition for Products in Semi-Permeable Containers

The guidance suggests that the intermediate condition should be 30°C/60% RH. A more appropriate condition for stressing the product would be 30°C NMT 40% RH.

Use of Statistical Analysis in Determining Retest or Shelf-Life

While statistical analysis is acceptable for determining expiry dates at initial filing, the use of this to extend dates without term data should be considered. At present, term data is required for extending retest or shelf-lives.

Acceptance Limits for Drug Substance

The guidance states that "Acceptance criteria should relate to the release limits to be derived from consideration of all available stability information.... It should include specific upper limits for degradation products, the justification for which should be influenced by levels observed in material used in preclinical and clinical studies....." Current experience suggests that preclinical and clinical limits do not play a significant role in assignment of specifications agreed at approval.

Drug Product Batches: Scale

The guidance states that two batches must be at least pilot-scale and a third may be smaller; lab-scale batches are not acceptable for formal stability studies. More clarity is needed to distinguish lab-scale from batches that are smaller than pilot-scale, such as "all batches must be manufactured using equipment of similar operating design and principle".

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